

Fig. 1

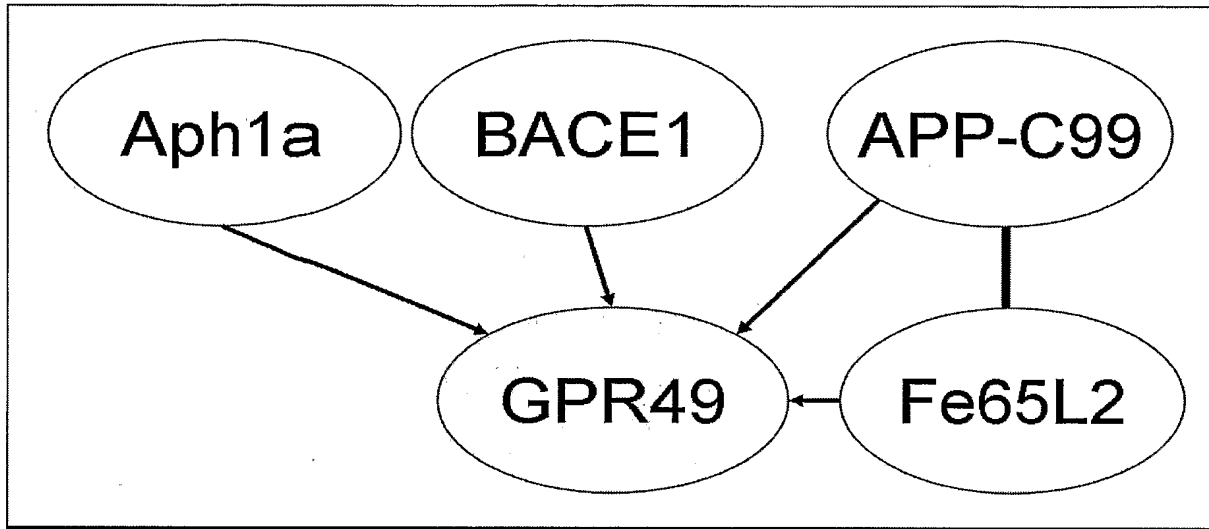


Fig. 2

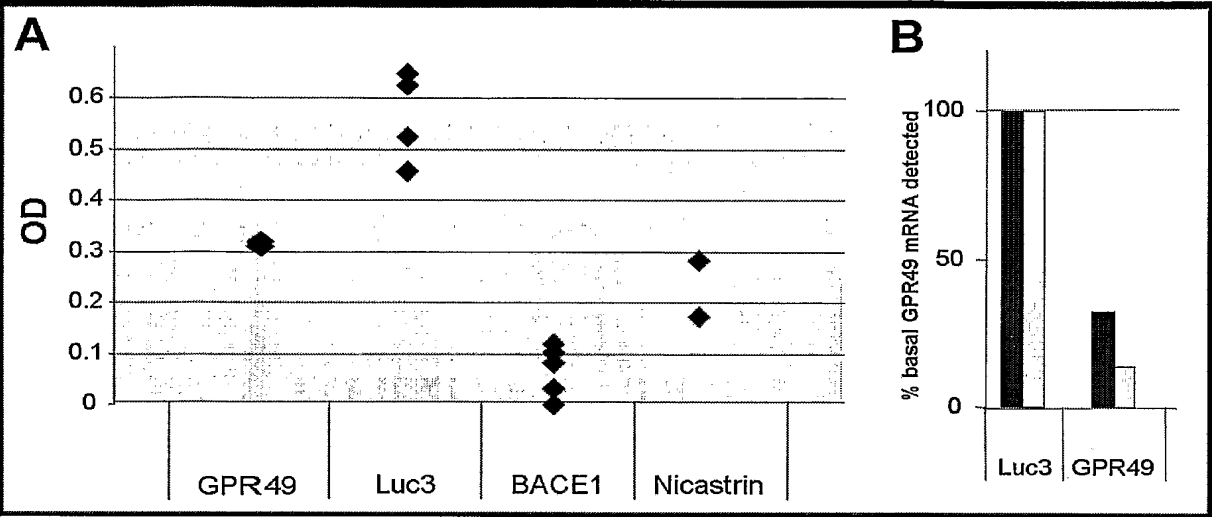


Fig. 3

	MDTSRLGVLL	SLPVLLQLAT	GGSSPRSGVL	LRGCPHCHC	EPDGRMLLRV
	DCSDLGLSEL	PSNLSVFYSY	LDLSMNNISQ	LLPNPLPSLR	FLEELRLAGN
5	ALTYIPKGAF	TGLYSLKVLM	LQNNQLRHVP	TEALQNLRLS	QSLRLDANHI
	SYVPPSCFSG	LHSLRHLWLD	DNALTEIPVQ	AFRSLSALQA	MTLALNKIHH
	IPDYAFGNLS	SLVVLHLHNN	RIHSLGKKCF	DGLHSLETLD	LNYYNNLDEFP
	TAIRTLNLK	ELGFHSNNIR	SIPEKAFVGN	PSLITIHFYD	NPIQFVGRSA
	FQHLPELRTL	TLNGASQITE	FPDLTGTANL	ESLTILTGAQI	SSLPQTVCNQ
10	LPNLQVLDLS	YNLLEDLPSF	SVCQKLQKID	LRHNEIYEIK	VDTFQQLLSL
	RSLNLAWNKI	AIHPNAFST	LPSLIKLDLS	SNLLSSFPIIT	GLHGLTHLKL
	TGNHALQSLI	SSENFPELKV	IEMPYAYQCC	AFGVCENAYK	ISNQWNKGDN
	SSMDDLHKKD	AGMFQAQDER	DLEDFLLD FE	EDLKALHSVQ	CSPSPGPFKP
	CEHLLDGWLI	RIGVWTIAVL	ALTCNALVTS	TVFRSPLYIS	PIKLLIGVIA
15	AVNMLTGVSS	AVLAGVDAFT	FGSFARHGAW	WENGVGCHVI	GFLSIFASES
	SVFLLTLAAL	ERGFSVKYSA	KFETKAPFSS	LKVIILLCAL	LALTMAAVPL
	LGGSKYGASP	LCLPLPFGEF	STMGYMVALI	LLNSLCFLMM	TIAYTKLYCN
	LDKGDLENIW	DCSMVKHIAL	LLFTNCILNC	PVAFLSFSSL	INLTFISPEV
	IKFILLVVVP	LPACLNPLLY	ILFNPHEFKED	LVSLRKQTYV	WTRSKHPSLM
20	SINSDDVEKQ	SCDSTQALVT	FTSSSITYDL	PPSSVPSPAY	PVTESCHLSS
	VAFVPCL				

Fig. 4 (1/2)

5	LGR5	MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPHCHCEPDGRMLLRVDCSDLGLSELPSNLSVFTSYLDLSMNNISQ
	LGR6	-----MRLEGEGRSARAGQNLRSAGSARRGAPR-----DLSMNNLTFE
	LGR4	-----MPGPLGLLCFLALGLLGSAGPSGAAPPLCAAPCSCDGRDR-----VDCSGKGLTAVPEGLSAFTQALDISMNNITQ
	Consensus/80%b.L.h.Gpts.tG....sss.pps.sc.....DlSMNNl*p
10	LGR5	LLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSKVLMLQNNQLRHVPTEALQNLRSLSQLRLDANHISYVPPSCFSG
	LGR6	LQPGLFHHLRFLEELRLSGNHLSHIPGQAFSGLYSLKILMLQNNQLGGIPAEALWELPSLQSL-----
	LGR4	LPEDAFKNFPFLEELQLAGNDLSFIHPKALSGLKELKVLTLQNNQLKTVPSEAIRGLSALQSLRLDANHITSVPEDSFEG
	Consensus/80%	L..s.b.pb.FLEELpLtGN.L*aI...Ab*GLbpLKlLhLQNNQL.hlpSEAlb.L.tLQSL.....
15	LGR5	LHSLRHLWLDNALTEIPVQA.FRSLSALQAMTLALNKIHHIPDYAFGNLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLD
	LGR6	-----D
	LGR4	LVQLRHLWLDNSLTEVPVHP.LSNLPTLQALTALNKKISSIPDFAFTNLSSLVVLHLHNNKIRLSQHCDFGLDNLLETLD
	Consensus/80%D
20	LGR5	LNYNLDEFPTAIRTLNLKE.LGFHSNNIRSIPEKAFVGNPSLITIHFDNPIQFVGRSAFQHLPELRLTLNGASQITE
	LGR6	LNYNLQEFFVAIRTLGRQLQELGFHNNNIKAPEKAFMGNPPLQTIHFYDNPIQFVGRSAFQYLPKLHLTLNGAMDIOE
	LGR4	LNYNLGEFFQAIALPSLKE.LGFHSNSISVIPDGAFDGNPLLRITIHLYDNPLSFVGNSAFHNSDLHSLVIRGASMVQQ
	Consensus/80%	LNYNpL.EFP.AI+sLspLpELGFHsNpsIP-.AF.GNP.LbTIHbYDNPlpFVGpSAFp.LscL+*LslpGA..lpp
25	LGR5	FPDLTGTANLESITLTGAQISSLPQTVCNQLPNLQVLDLSYNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSL
	LGR6	FPDLKGTTSLEIITLFRAGIRLLPSGMCQQLPRLRVLELSHNQIEELPSLHRCQKLEEIQLQHNRIWEIGADTFQQLSSL
	LGR4	FPNLTGTVHLESITLTGTKISSIPNNLCQEQKMLRTLDLSYNNIRDLPFNGCHALEEISLQRNQIYQIKEGTFQGLISL
	Consensus/80%	FpSLpGTspLE.LTLT.s.Ip.lPpshCpbb..LpsL-LSaN.lc-LPSbp.Cp.LpcIsLp+NpIapI..stFp.L.SL
30	LGR5	RSNLAWNKIAIHPNAFSTLPSLIKDLSSNLLSSFFITGLHGLTHLKLGTGNHALQSLISSENFPELKVIMPYAYQCC
	LGR6	QALDLSWNAIRSIHPEAFSTLHSLVKLDLTDNQLTTLPLAGLGGLMHLKLKGNLALSQAFSKDSFPKLRILEVPIYAYQCC
	LGR4	RILDLSRNLIHEIHSRAFATLGPITNLDVSFNETLSFPTEGLNGLNQLKLVGNFKLKEALAADFVNRLSLSVPYAYQCC
	Consensus/80%	p.LsLtbN.I..IHspAFTTL.sIhpLDl*.NbL**bPh.GL.GL.pLKL.GNb.Lpphbt.csFspL+.lphPYAYQCC
35	LGR5	AFGVCENAYKISNQWNGDNS SMDD-LHKKDAGMFOAQDE----RDLEDFLLDFEEDLKALHSVQCSPSPGFFKPCHELL
	LGR6	PYGMCAFFKASGQWEAEDLHLDDEESSKRPLGLLARQAENHYDQDLDELQLEMEDS-KPHPSVQCSPTPGFFKPCYLF
	LGR4	AFWGCDSYANLN----TEDNSLQDHSVAQEKGKCMSTADA-----ANVTSTLENEEHSQIIHCTPSTGAFKPCYLL
	Consensus/80%	sahhC.shhphs.....D.p..Dc...pc.h.hb...s.....ph..pbEpp.+sb..lpC*P*sGsFKPCEaLb
40	LGR5	DGWLIRIGVWTIAVLALTCNALVTSTVFR-SPLYISPIKLLIGVIAAVNMLTGVSSAVLAGVDAFTFGSFARHGAWENG
	LGR6	ESWGIRLAVWAIVLLSVLCNGLVLLTVFAGGPVPLPPVKFVVGAAGANTLTGISCGLLASVDALTFGQFSEYGARWETG
	LGR4	GSWMIRLTVWFIFLVALFFNLVLILTTFASCTSLPSSKLFGLISVSNLFGMIYTGILTFDAVSWGRFAEFGIWWETG
	Consensus/80%	.tWhIRIsVWhIhltlhhNhLVh.TsF..tsh.lss.KbhlGhItssNhbhGl.stlLs.lDAh*aGpFtcaGhbWESG

continued as Fig. 4 (2/2)

Fig. 4 (2/2)

continued from Fig. 4 (1/2)

5

LGR5 VGCHVIGFLSIFASESSVFLTLAALERGFVSVKYSAKFETKAPFSSLKVIILLCALLALTMAAVPLGGSKYGASPLCLP
LGR6 LGCRATGFLAVLGSEASVLLTLAAVQC SVSVCVRAYGKSPSLG SVRAGVLGCLALAGLAAALPLASVGEYGASPLCLP
LGR4 SGCKVAGFLAVFSSESAILFLMLATVERSLSAKDIMKNGKSNHLKQFRVAALLAFLGATVAGCFPLFHRGEYSASPLCLP
Consensus/80% .GC+shGFLtltbtSEttlbLLhLaslppthSsp.....pps.b.ph+shhLhshhhAhhtshPLh..tcYtASPLCLP

10

LGR5 --LPFGEPSTMGYVALIILLNSLCFLMMTIAYTKLYCNLDKGDLENIWDCSMVKHIALLLFTNCILNCPVAFLSFSSLIN
LGR6 YAPPEGQPAALGFTVALVMNSFCFLVAGAYIKLYCDLPRGDFEAVWDCAMVRHVAVLI FADGLLYCFVAFLSFASMLG
LGR4 --FPTGETPSLGFTTVTLVLLNSLAFLMAVIYTKLYCNLEKEDLSENSQSSMIKHVAVLI FTNCIFFCFVAFFSFAPLIT
Consensus/80% ...P.GpsssbGahVsLlbbNSbsFLhshhYhKLYCsL.+Dbp...pstMl+HlAbLiFssslb.CPVAFbSftsbls

15

LGR5 LTFISPEVIK FILLVVVPLPACLNPLLYILFNPHEKEDLVSLRKQTYVWTRSKHPSLMSINSDDVEKQSCDS-----TQ
LGR6 LFPVTPEAVKSVLLVVLPLPACLNPLLYLLFNPHERDDLRLRLPR-----AGDSGLAYAAAGELEKSSCDs-----TQ
LGR4 AISISPEIMKSVTLIFFPLPACLNPLVLYVFFNPFKEDWKLLKRRVTKKSGSVSVSISSQGGCLEQDFYYDCGMYSHLQG
Consensus/80% hh.1*PEhhK.lhLlhhPLPACLNPLLYlbFNP+F+-Db..L+.p.....t.pssl...sts..pc..hDs.....p.

20

LGR5 ALVFTTSSSITYDLPPS-----SVFPAYPVTESCHLS-----
LGR6 ALVAFSDVDLILEASEAGRPPGLETYGFPSVTLISCQQPGAPRLEGSHCVEPEGNHFGNPQPSMDGELLRLAEGSTPAGG
LGR4 NLTVDCCESEFLTKPVSCKHLIKSHSCPALAVASCQRPEGYWSDCGTQSAHSDYADEEDSFVSDSSDQVQACGRACFYQ
Consensus/80% sLshsssp.hb.h.s.....Ss.pP.h...-ssp.s.....

25

LGR5 -----SVAFPCL
LGR6 GLSGGGGFQPSGLAFASHV
LGR4 SRGFPLVRYAYNLPRVKD-
Consensus/80%slsbs.p.

30